



UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
05/483,539	10/22/99	DEAN	N ISIS-3013

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HZ12/0328

EXAMINER

SHIBUYA, M

ART UNIT	PAPER NUMBER
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1635

DATE MAILED: 03/28/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/403,539

Applicant(s)

DEAN ET AL.

Examiner

Mark Shibuya

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 January 2001.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 8, 10-18, 27-29 and 31-33 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 8, 10-18, 27-29 and 31-33 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f):
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☐ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 18) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other: _____

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DETAILED ACTION

Response to Arguments

1. The applicants' response filed 1/18/00^{01 KSS}, has been considered. Rejections and/or objections not reiterated from the previous office action mailed 10/18/00, are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

Priority

2. Acknowledgment is made of applicant's reference that the instant application is a continuation-in-part of Serial No. 08/847,151, filed 4/30/97.

Information Disclosure Statement

3. Acknowledgment is made of applicant's provision of the return postcard indicating receipt of all cited references by the PTO mailroom on April 24, 2000. The examiner has personally searched for the missing references and has been unable to find them. If the applicant remains willing to cooperate with the examiner to locate replacement copies thereof, the examiner would be grateful for such cooperation. The examiner apologizes for this inconvenience to the applicant.

a. No copies have been furnished to the examiner for consideration of applicant's references: AE, AG, AH, AI, AO, AS AT, AU, BA, BM, BX, and CD. The examiner request that the applicant furnish these references, although applicant apparently has already furnished these references to the U.S. Patent and Trademark Office, and thanks the applicant for their cooperation.

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Double Patenting

4. Claims 1, 8 and 10 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 5,789,573 (filed 5/24/96). This rejection is maintained for the reasons of record as set forth in the previous Office action, mailed 10/18/00.

5. Claims 1, 8 and 10 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 5,789,573 (filed 5/24/96). This rejection is maintained for the reasons of record as set forth in the previous Office action, mailed 10/18/00.

6. Claims 10-16 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 5,789,573 in view of Milligan et al., Kahne, (U.S. Patent No. 5,795,870), and Carrano et al., (U.S. Patent No. 5,739,118).

7. These rejections over the claims of U.S. Patent No. 5,789,573 are maintained for the reasons of record as set forth in the previous Office action, mailed 10/18/00. Applicant does not necessarily agree with the rejections but does not present substantive arguments against the rejection. Applicant's confirmation pursuant to 37 C.F.R. 1.78(c) is acknowledged.

8. Claims 17 and 18 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 5-7 of U.S. Patent No. 6,087,489 (filed 6/2/98). This rejection is maintained for the reasons of record as set forth in the previous Office action, mailed 10/18/00. Applicant does not necessarily agree with the rejection but does not

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present substantive arguments against the rejection. Applicant's confirmation pursuant to 37 C.F.R. 1.78(c) is acknowledged.

9. Claims 27, 28, 31, 32, and 33 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 21 and 28-32 of copending Application No. 08/847,151. This rejection is maintained for the reasons of record as set forth in the previous Office action, mailed 10/18/00. Applicant does not necessarily agree with the rejection but does not present substantive arguments against the rejection.

Claim Rejections - 35 U.S.C. § 112

10. Claims 27-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of modulating expression of a target nucleic acid comprising administering into the alimentary canal an effective amount of an oligonucleotides comprising 2'-O-alkyl or 2'-O-alkoxy modifications, does not reasonably provide enablement for methods of inhibiting gene expression by the oral administration of oligonucleotides that do not comprise 2'-O-alkyl or 2'-O-alkoxy modifications. This rejection is maintained for the reasons of record as set forth in the previous Office action, mailed 10/18/00.

a. Applicant argues that the Office action identifies problems with the claimed methods and criticizes the specification for allegedly not addressing these problems. Applicant asserts that such problems are actually to be expected, and do not negate patentability. The applicant asserts that it is improper for the PTO to require any showing regarding the degree of effectiveness of therapeutic invention, relying upon MPEP section 2107.02; In re Sichert, 566 F.2d 1154

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(C.C.P.A. 1977); In re Brana, 51 F.3d 1560, 1567-68 (Fed. Cir. 1995). Applicant states that “to the extent that ‘problems’ are identified, such ‘problems’ relate to optimizing the performance of a therapeutic product, and not to simply obtaining measurable results. Since there is no requirement that an invention be optimized to be patentable, the references cited in the Office Action fail to support rejection of Applicants’ claims.”

b. Applicant’s arguments have been fully considered but are not deemed persuasive. As best understood, applicant argues that the claims have been rejected for no showing of pharmaceutical efficacy. However, the standard under which the claims have been rejected is that the undue experimentation would be required of one of skill in the art to make and use the claimed invention commensurate in scope with these claims. As stated in the previous rejection, the art of oral administration of antisense oligonucleotides is unpredictable. The references were cited for this proposition. Furthermore, the specification does not provide particular guidance or direction for overcoming this unpredictability.

Claim Rejections - 35 U.S.C. § 102

11. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

12. Claims 1, 8 and 10 are rejected under 35 U.S.C. 102(e) as being anticipated by Baker et al., U. S. Patent No. 5,789,573. This rejection is maintained for the reasons of record as set forth in the previous Office action, mailed 10/18/00.

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a. The claims are drawn to an oligonucleotide that comprises at least one heteroatomic backbone modification and a 2'-alkoxyalkoxy modification.

b. Applicant cites In re Arkley, 455 F.2d 586, 587 (C.C.P.A. 1972) in support applicant's argument that the anticipatory reference U. S. Patent No. 5,789,573 does not "clearly and unequivocally disclose the claimed [invention] or direct those skilled in the art to the [invention] without *any* need for picking, choosing and combining various disclosures not directly related to each other by the teaching of the cited reference."

c. Applicant's arguments have been considered but are not deemed persuasive. Table 1 in column 6 explicitly teaches oligonucleotides that comprise at least one heteroatomic backbone modification and a 2'-alkoxyalkoxy modification.

13. Claims 17 and 18 were rejected under 35 U.S.C. 102(e) as being anticipated by Dean, Patent No.6,087,489. This rejection is withdrawn in view of applicant's arguments as set forth in the first paragraph on p. 7 of the response to the previous Office action.

Claim Rejections - 35 U.S.C. § 103

14. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

15. Claims 1, 8, and 10-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hanecak et al., in view of Milligan et al., Kahne, (U.S. Patent No. 5,795,870), and Carrano et al., (U.S. Patent No. 5,739,118). This rejection is maintained for the reasons of record as set forth in the previous Office action, mailed 10/18/00.

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a. The claims are directed to pharmaceutical compositions comprising the oligonucleotide of claim 1 and various penetration enhancers.

b. As best understood, applicant argues that the Carrano reference teaches placement of an antisense molecule in an expression vector, so that the combination with the Hanacek reference, which discloses 2'-alkoxyalkyl-substituted oligonucleotides, would result in an expression vector containing the Hanacek oligonucleotide.

c. Applicant's arguments have been carefully considered but are not deemed persuasive. As set forth in the previous Office action, the Carrano reference was cited for delivery of antisense nucleic acids in a composition comprising various penetration enhancers. Applicant has not pointed to how delivery of the oligonucleotides of the claimed invention would exhibit a result that was unexpected when delivered in the composition taught by Carrano for the delivery of antisense nucleic acid vectors. It is unlikely that any such unexpected result would occur, because facilitated delivery of nucleic acids in composition comprising penetration enhancers would be expected to occur, regardless if the nucleic acid happened to be an oligonucleotide or a vector. Absent evidence to the contrary, penetration enhancers would work given the chemical composition of the nucleic acid as a nucleic acid, and not whether the nucleic acid was an oligonucleotide or a vector.

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Conclusion

16. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

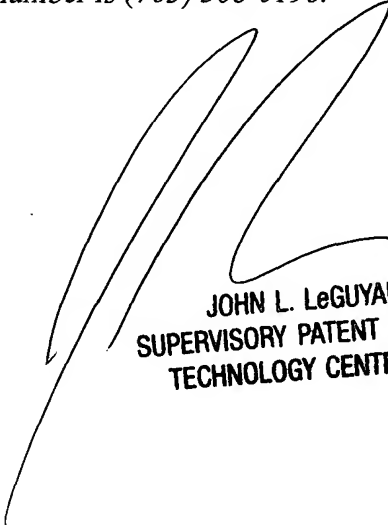
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to *Mark L. Shibuya (SRC)*, whose telephone number is (703) 308-9355, and/or to the patent analyst, *Katrina Turner*, whose telephone number is (703) 305-3413.

18. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *John LeGuyader* may be reached at (703) 308-0447.

19. Any inquiry of a general nature or relating to the status of this application should be directed to the *Group receptionist* whose telephone number is (703) 308-0196.

Mark L. Shibuya
Patent Examiner
Technology Center 1600
March 18, 2001



JOHN L. LeGUYADER
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600